

1008860 2

PCT/US00/21974

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE  
in its capacity as elected Office

|  |  |
|--|--|
| Date of mailing (day/month/year)<br>15 August 2001 (15.08.01)              |  |
| International application No.<br>PCT/US00/21974                            | Applicant's or agent's file reference<br>X-11506               |
| International filing date (day/month/year)<br>18 September 2000 (18.09.00) | Priority date (day/month/year)<br>27 September 1999 (27.09.99) |
| Applicant<br>LUKE, Wayne, Douglas  |  |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
27 March 2001 (27.03.01)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).


|   |  |
|---|--|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br>Facsimile No.: (41-22) 740.14.35 | Authorized officer<br>Maria Kirchner<br>Telephone No.: (41-22) 338.83.38 |
|---|--|

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

10/088002

|  |   |  |
|--|---|--|
| Applicant's or agent's file reference<br>X-11506   | <b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |  |
| International application No.<br>PCT/US00/21974  | International filing date (day/month/year)<br>18/09/2000  | Priority date (day/month/year)<br>27/09/1999 |
| International Patent Classification (IPC) or national classification and IPC<br>C07D295/08   |   |  |
| Applicant<br>ELI LILLY AND COMPANY et al.  |   |  |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>  |   |  |
| <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"><li>I <input checked="" type="checkbox"/> Basis of the report</li><li>II <input type="checkbox"/> Priority</li><li>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li><li><input type="checkbox"/> Lack of unity of invention</li><li><input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li><li><input type="checkbox"/> Certain documents cited</li><li><input type="checkbox"/> Certain defects in the international application</li><li><input type="checkbox"/> Certain observations on the international application</li></ul> |   |  |
| Date of submission of the demand<br><br>27/03/2001   | Date of completion of this report<br><br>22.02.2002   |  |
| Name and mailing address of the international preliminary examining authority:<br><br> European Patent Office - P.B. 5818 Patentlaan 2<br>NL-2280 HV Rijswijk - Pays Bas<br>Tel. +31 70 340 - 2040 Tx: 31 651 epo nl<br>Fax: +31 70 340 - 3016  | Authorized officer<br><br>Pauwels, G<br><br>Telephone No. +31 70 340 2379   |  |



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/21974

## I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-26 as originally filed

**Claims, No.:**

1-14 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/21974

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

|                               |      |        |      |
|-------------------------------|------|--------|------|
| Novelty (N)                   | Yes: | Claims | 1-14 |
|                               | No:  | Claims |      |
| Inventive step (IS)           | Yes: | Claims |      |
|                               | No:  | Claims | 1-14 |
| Industrial applicability (IA) | Yes: | Claims | 1-14 |
|                               | No:  | Claims |      |

2. Citations and explanations  
**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

---

International application No. PCT/US00/21974

Reference is made to the following document:

D1: EP-A-0699672

Re Item I

Basis of the opinion

The examination is being carried out on the following application documents:

Text for the Contracting States:

AT BE CH DE DK ES FI FR GB GR IT IE LI LU MC NL PT SE

Description, pages:

1-26 as originally filed

Claims, No.:

1-14 as originally filed

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1 The document D1 is regarded as being the closest prior art to the subject-matter of claim 1, and discloses (cf claim 1; page 8: lines 23 - 27): A process for preparing a 4-aminoalkoxy benzoic ester of formula (I) by reacting a haloalkylamine of formula (II) with a 4-hydroxybenzoic ester in the presence of an inorganic base.

The subject-matter of claim 1 therefore differs from this known process in that a hydrated inorganic base is used.

- 2 The problem to be solved by the present invention may therefore be regarded as to provide a further process for preparing a 4-aminoalkoxy benzoic ester of formula (I).

The solution proposed in claim 1 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons.

- 2.1 The present description (page 3, first paragraph) alleges that the teaching of the prior art is limited to the use of anhydrous powdered potassium carbonate, which role would be crucial. However, the skilled person clearly learns from the cited passage on page 8 of D1 that, although powered potassium carbonate is considered as the most efficient in the process, other organic and inorganic bases are suitable as well. The teaching of D1 is thus not limited to the use of powered anhydrous potassium carbonate only, but includes the use of all organic and inorganic bases. On the basis of the disclosure in D1, it is not clear what would refrain the skilled person from using other bases than anhydrous powdered potassium carbonate in the process of D1.
- 2.2 The subject-matter of claim 1 consists thus in the selection of hydrated bases from the bases described in document D1. Such a selection can only be regarded as inventive, if the hydrated bases presents unexpected effects or properties in relation to the rest of the range. However, no such effects or properties are indicated in the application. Hence, no inventive step is present in the subject-matter of claim 1.
- 2.3 Claims 2 to 14 apparently concern obvious alternative processes to the process of claim 1, an inventive step could only be recognized for these claims, if they relate to a new and inventive independent claim.

## PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

GINAH, F.O.  
ELI LILLY AND COMPANY  
Lilly Corporate Center  
Indianapolis Indiana 46285  
ETATS-UNIS D'AMERIQUE

PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT  
(PCT Rule 71.1)

Date of mailing  
(day/month/year) 22.02.2002

Applicant's or agent's file reference  
X-11506

## IMPORTANT NOTIFICATION

International application No.  
PCT/US00/21974

International filing date (day/month/year)  
18/09/2000

Priority date (day/month/year)  
27/09/1999

Applicant  
ELI LILLY AND COMPANY et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

## 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office - P.B. 6818 Patentlaan 2  
NL-2280 HV Rijswijk - Pays Bas  
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl  
Fax: +31 70 340 - 3016

Authorized officer

Smits, A

Tel. +31 70 340-3596





## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

|  |   |   |
|--|---|---|
| Applicant's or agent's file reference<br><b>X-11506</b>  |   | <b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)   |
| International application No.<br><b>PCT/US00/21974</b>   | International filing date (day/month/year)<br><b>18/09/2000</b> | Priority date (day/month/year)<br><b>27/09/1999</b>   |
| International Patent Classification (IPC) or national classification and IPC<br><b>C07D295/08</b>  |   |   |
| Applicant<br><b>ELI LILLY AND COMPANY et al.</b>   |   |   |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>  |   |   |
| <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I <input checked="" type="checkbox"/> Basis of the report</li> <li>II <input type="checkbox"/> Priority</li> <li>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV <input type="checkbox"/> Lack of unity of invention</li> <li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI <input type="checkbox"/> Certain documents cited</li> <li>VII <input type="checkbox"/> Certain defects in the international application</li> <li>VIII <input type="checkbox"/> Certain observations on the international application</li> </ul> |   |   |
| Date of submission of the demand<br><b>27/03/2001</b>  |   | Date of completion of this report<br><b>22.02.2002</b>  |
| Name and mailing address of the international preliminary examining authority:<br> European Patent Office - P.B. 5818 Patentlaan 2<br>NL-2280 HV Rijswijk - Pays Bas<br>Tel. +31 70 340 - 2040 Tx: 31 651 epo nl<br>Fax: +31 70 340 - 3016  |   | Authorized officer<br><br><b>Pauwels, G</b><br><br>Telephone No. +31 70 340 2379<br> |



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/21974

**I. Basis of the report**

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17):*)

Description, pages:

1-26 as originally filed

Claims, No.:

1-14 as originally filed

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/21974

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, Inventive step or Industrial applicability; citations and explanations supporting such statement**

**1. Statement**

|                               |                  |
|-------------------------------|------------------|
| Novelty (N)                   | Yes: Claims 1-14 |
|                               | No: Claims       |
| Inventive step (IS)           | Yes: Claims      |
|                               | No: Claims 1-14  |
| Industrial applicability (IA) | Yes: Claims 1-14 |
|                               | No: Claims       |

**2. Citations and explanations**  
**see separate sheet**

**INTERNATIONAL PRELIMINARY**

International application No. PCT/US00/21974

**EXAMINATION REPORT - SEPARATE SHEET**

---

Reference is made to the following document:

D1: EP-A-0699672

**Re Item I**

Basis of the opinion

The examination is being carried out on the following application documents:

Text for the Contracting States:

AT BE CH DE DK ES FI FR GB GR IT IE LI LU MC NL PT SE

Description, pages:

1-26 as originally filed

Claims, No.:

1-14 as originally filed

**Re Item V**

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1 The document D1 is regarded as being the closest prior art to the subject-matter of claim 1, and discloses (cf claim 1; page 8: lines 23 - 27): A process for preparing a 4-aminoalkoxy benzoic ester of formula (I) by reacting a haloalkylamine of formula (II) with a 4-hydroxybenzoic ester in the presence of an inorganic base.

The subject-matter of claim 1 therefore differs from this known process in that a hydrated inorganic base is used.

- 2 The problem to be solved by the present invention may therefore be regarded as to provide a further process for preparing a 4-aminoalkoxy benzoic ester of formula (I).

**INTERNATIONAL PRELIMINARY**

International application No. PCT/US00/21974

**EXAMINATION REPORT - SEPARATE SHEET**

---

The solution proposed in claim 1 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons.

- 2.1 The present description (page 3, first paragraph) alleges that the teaching of the prior art is limited to the use of anhydrous powdered potassium carbonate, which role would be crucial. However, the skilled person clearly learns from the cited passage on page 8 of D1 that, although powdered potassium carbonate is considered as the most efficient in the process, other organic and inorganic bases are suitable as well. The teaching of D1 is thus not limited to the use of powdered anhydrous potassium carbonate only, but includes the use of all organic and inorganic bases. On the basis of the disclosure in D1, it is not clear what would refrain the skilled person from using other bases than anhydrous powdered potassium carbonate in the process of D1.
- 2.2 The subject-matter of claim 1 consists thus in the selection of hydrated bases from the bases described in document D1. Such a selection can only be regarded as inventive, if the hydrated bases presents unexpected effects or properties in relation to the rest of the range. However, no such effects or properties are indicated in the application. Hence, no inventive step is present in the subject-matter of claim 1.
- 2.3 Claims 2 to 14 apparently concern obvious alternative processes to the process of claim 1, an inventive step could only be recognized for these claims, if they relate to a new and inventive independent claim.

# TENT COOPERATION TREATY

# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

|  |   |  |
|--|---|--|
| Applicant's or agent's file reference<br><b>X-11506</b>  | <b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. |  |
| International application No.<br><b>PCT/US 00/ 21974</b> | International filing date (day/month/year)<br><b>18/09/2000</b>   | (Earliest) Priority Date (day/month/year)<br><b>27/09/1999</b> |
| Applicant<br><br><b>ELI LILLY AND COMPANY et al.</b>     |   |  |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No. \_\_\_\_\_



as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.



None of the figures.

# INTERNATIONAL SEARCH REPORT

International Application No

PC/JS 00/21974

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D295/08 C07D333/56

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

PAJ, WPI Data, CHEM ABS Data, EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages                        | Relevant to claim No. |
|------------|---|-----------------------|
| X          | EP 0 699 672 A (LILLY CO ELI)<br>6 March 1996 (1996-03-06)<br>cited in the application<br>claims<br>----- | 1-14                  |

☐

Further documents are listed in the continuation of box C.

☒

Patent family members are listed in annex.

\* Special categories of cited documents :

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*G\* document member of the same patent family

Date of the actual completion of the international search

12 July 2001

Date of mailing of the international search report

20/07/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Pauwels, G

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/21974

| Patent document<br>cited in search report | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|---|---------------------|----------------------------|---------------------|
| EP 0699672 A                              | 06-03-1996          | US 5631369 A               | 20-05-1997          |
|   |                     | AT 165355 T                | 15-05-1998          |
|   |                     | BR 9503846 A               | 17-09-1996          |
|   |                     | DE 69502152 D              | 28-05-1998          |
|   |                     | DE 69502152 T              | 17-09-1998          |
|   |                     | DK 699672 T                | 07-10-1998          |
|   |                     | ES 2114721 T               | 01-06-1998          |
|   |                     | FI 954067 A                | 01-03-1996          |
|   |                     | GR 3026742 T               | 31-07-1998          |
|   |                     | HK 1006912 A               | 19-03-1999          |
|   |                     | HU 73141 A                 | 28-06-1996          |
|   |                     | JP 8119964 A               | 14-05-1996          |
|   |                     | US 5750688 A               | 12-05-1998          |